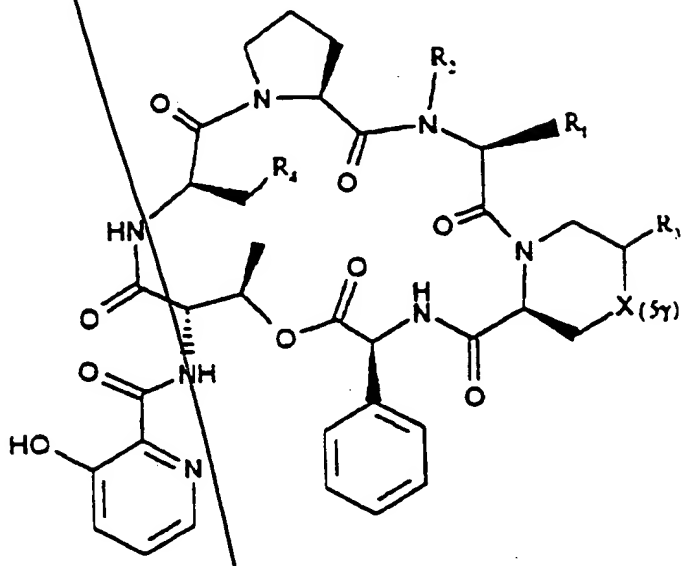
CLAIMS

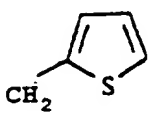
1. Compound characterized in that it is represented by the general formula I

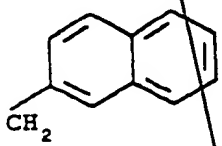


I

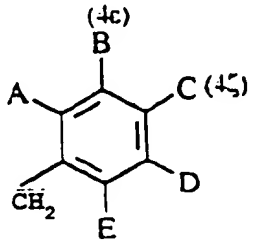
in which:

- R_2 and R_4 represent, independently of each other, a hydrogen atom or a methyl group,
- R_3 represents a hydrogen atom or a hydroxyl group,
- X represents a CO, CHOH or CH_2 group, and
- R_1 represents:





or



with

- <u>for the m ta derivatives:</u>

A, C, D and E representing a hydrogen atom, and

B being able to repres nt:

- a halogen, and preferably a fluorine atom,
- a monoalkylamino or dialkylamino group,

with alkyl preferably representing a methyl or ethyl group,

- an ether group,
- a thioether group,
- a C_1 to C_3 alkyl group, or
- a trihalogenomethyl group, preferably trifluoromethyl.

- <u>for the para derivatives:</u>

A, B, D and E representing a hydrogen atom, and

C being able to represent:

- a halogen,
- an NR_1R_2 group with R_1 and R_2 representing, independently of each other, a group selected from among
  - hydrogen,
  - a straight-chain or branched C_1 to C_4 alkyl group where, when one of the substituents R_1 or R_2 represents a methyl group, the other necessarily represents an ethyl group,
  - an alkyl-cycloalkylmethyl group with a C_3 to C_4 cycloalkyl,
  - an optionally substituted C_3 to C_4 cycloalkyl group,

- a straight-chain or branch d C_1 to C_4 alkenyl group where, when one of the substituents R_1 or R_2 represents an alkenyl group, the other is different from a methyl group or a C3 to C6 cycloalkyl group,

- a substituted or unsubstituted N-pyrrolidinyl group,

- an ether group,

- a thioether group,

- an acyl or alkoxycarbonyl group,

- a C_1 to C_6 alkyl group which is straight-chain or branched and which is preferably selected from among the methyl, isopropyl and tert-butyl groups,

- an alkylthiomethyl group,

- an aryl group, preferably a phenyl group, or

- a trihalogenomethyl group, preferably trifluoromethyl and

- <u>for the meta-para disubstituted derivatives:</u>

A, D and E representing a hydrogen atom, and

B being able to represent:

- a halogen, preferably a fluorine atom,

- a monoalkylamino or dialkylamino group with alkyl preferably representing a methyl or ethyl group,

- an ether group,

- a thioether group,

- a C_1 to C_3 alkyl group, and

C being able to represent:

- a halogen, and preferably a fluorine atom,

- an amino, monoalkylamino or dialkylamino group with alkyl preferably representing a methyl group with the proviso that B is different from a bromin or chlorine atom, or a substituted or unsubstituted allyl group,

- an ether group,

- a thioether group,

- a C_1 to C_6 alkyl group, or

- a trihalogenomethyl group, preferably trifluoromethyl, and

- <u>for the ortho-para disubstituted derivatives:</u>

B, E and D representing a hydrogen atom and A and C a methyl group.

2. Compound according to claim 1, characterized in that it is preferably:

4ζ-methylthio-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-methylthio-de(4ζ-dimethylamino)pristinamycin I_B,

5γ-hydroxy-4ζ-methylthio-de(4ζ-dimethylamino)pristinamycin I_B,

4ζ-methyl-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-methyl-de(4ζ-dimethylamino)pristinamycin I_B,

4ζ-methoxy-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-methoxycarbonyl-

d (4ζ-dim thylamino)pristinamycin I_A,

4ζ-chloro-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-bromo-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-bromo-de(4ζ-dimethylamino)pristinamycin I_B,

4ζ-iodo-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-iodo-de(4ζ-dimethylamino)pristinamycin I_B,

4ζ-trifluoromethyl-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-trifluoromethyl-de(4ζ-dimethylamino)-pristinamycin I_B,

4ζ-tert-butyl-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-isopropyl-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-isopropyl-de(4ζ-dimethylamino)-pristinamycin I_B,

4ε-methylamino-de(4ζ-dimethylamino)-pristinamycin I_A,

4ε-methoxy-de(4ζ-dimethylamino)pristinamycin IA,

4ε-methoxy-de(4ζ-dimethylamino)pristinamycin IH,

4ε-fluoro 4ζ-methyl-de(4ζ-dimethylamino)-pristinamycin IA,

4ζ-amino-de(4ζ-dimethylamino)pristinamycin IA,

4ζ-ethylamino-de(4ζ-dimethylamino)-

pristinamycin I_A,

4ζ-diethylamino-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-allylamino-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-diallylamino-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-allylethylamino-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-ethylpropylamino-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-ethylisopropylamino-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-ethylmethylcyclopropylamino-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-(1-pyrrolidinyl)-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-trifluoromethoxy-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-allyloxy-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-ethoxy-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-ethylthio-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-m thylthiomethyl-de(4ζ-dimethylamino)-pristinamycin I_A,

4ζ-(2-chloroethoxy)-de(4ζ-dimethylamino)-

pristinamycin I_A,

4ζ-acetyl-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-ethyl-de(4ζ-dimethylamino)pristinamycin I_A,

4ζ-ethyl-de(4ζ-dimethylamino)pristinamycin I_B,

4ε-dimethylamino-de(4ζ-dimethylamino)-pristinamycin I_A,

4ε-methylthio-de(4ζ-dimethylamino)-pristinamycin I_A, and

4ε-ethoxy-de(4ζ-dimethylamino)pristinamycin I_A.

3. Process for preparing streptogramins, characterized in that it employs a streptogramin-producing microorganism strain which possesses at least one genetic modification which affects the biosynthesis of a precursor of the group B streptogramins, and in that the said mutant strain is cultured on a culture medium which is appropriate and which is supplemented with at least one novel precursor which is different from that whose biosynthesis is altered, and in that the said streptogramins are recovered.

4. Process according to claim 3, characterized in that the mutant strain possesses at least one genetic modification which is located within one of the genes involved in the biosynthesis of the group B streptogramin precursors.

5. Process according to claim 4,

characterized in that the gene(s) whose expression is altered is/are selected from among the genes which are involved in the biosynthesis of L-2-aminobutyric acid, 4-dimethylamino-L-phenylalanine (DMPAPA), L-pipecolic acid, L-phenylglycine and/or 3-hydroxypicolinic acid.

6. Process according to claim 4 or 5, characterized in that at least one of the genes is selected from among the papA, papM, papC (SEQ ID No. 2), papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID No. 6) and hpaA (SEQ ID No. 8) genes.

7. Process according to one of claims 3 to 6, characterized in that the said genetic modification renders at least one of the genes involved in the biosynthesis of the group B streptogramin precursors partially or totally incapable of encoding the natural enzyme.

8. Process according to one of claims 3 to 7, characterized in that the genetic modification consists of a disruption of one of the genes involved in the biosynthesis of the group B streptogramin precursors.

9. Process according to one of the preceding claims, characterized in that the mutant strain employed is derived from the strain S. pristinaespiralis and preferably from the strain S. pristinaespiralis SP92.

10. Process according to claim 9, characterized in that the strain is preferably the

strain SP92:pVRC508.

11. Process according to claim 9, characterized in that the strain is preferably the strain SP212.

12. Process according to claim 9, characterized in that the strain is preferably the strain SP92pipA::Ωam^R.

13. Process according to claim 9, characterized in that the strain is preferably the strain SP92hpA::Ωam^R.

14. Process according to any one of the preceding claims, characterized in that the novel precursor, which is introduced into the culture medium, is selected from among derivatives or analogues of amino acids and alpha-ketocarboxylic acids.

15. Process according to any one of the preceding claims, characterized in that the novel precursor is preferably selected such that it is related to the precursor whose biosynthesis is altered.

16. Process according to claim 14 or 15, characterized in that the novel precursor is preferably a derivative of phenylalanine when the gene whose expression is altered relates to the biosynthesis of DMPAPA.

17. Process according to one of the preceding claims which is useful for preparing pristinamycin IB.

18. Nucleotide sequence, characterized in

that it is selected from among:

(a) all or part of the genes papC (SEQ ID No. 2), papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID No. 6) and hpaA (SEQ ID No. 8),

(b) sequences which hybridize with all or part of the (a) genes, and

(c) sequences which are derived from (a) and (b) sequences on account of the degeneracy of the genetic code.

19. Nucleotide sequence according to claim 18, characterized in that it is selected from among the papC (SEQ ID No. 2), papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID No. 6) and hpaA (SEQ ID No. 8) genes.

20. Recombinant DNA encompassing a gene selected from among the papC (SEQ ID No. 2), papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID No. 6) and hpaA (SEQ ID No. 8) genes.

21. Vector, characterized in that it encompasses a nucleotide sequence according to claim 18 or 19 or a recombinant DNA according to claim 20.

22. Use of a sequence according to claim 18 or 19 and/or of a vector according to claim 21 for preparing metabolites.

23. Polypeptide which results from the expression of a sequence according to claim 18 or 19.

24. Mutant S. pristinaespiralis strain, charact rized in that it possesses at least one genetic

modification within one of its papC (SEQ ID No. 2), papB (SEQ ID No. 3), pipA (SEQ ID No. 5), snbF (SEQ ID No. 6) and/or hpaA (SEQ ID No. 8) g nes.

25. Mutant strain according to claim 24, characterized in that it is the strain SP92pipA::Ωam^R.

26. Mutant strain according to claim 24, characterized in that it is the strain SP92hpaA::Ωam^R.

27. Mutant S. pristinaespiralis strain, characterized in that it possesses a genetic modification which consists of a disruption of the papA gene by double homologous recombination, such as SP212.

28. Compound, characterized in that it is 4-trifluoromethoxyphenylalanine, 3-methylaminophenylalanine, 3-methylthiophenylalanine, 3-fluoro-4-methylphenylalanine, 4-methylaminophenylpyruvic acid, 3-ethoxyphenylalanine, 4-allylaminophenylalanine, 4-diallylaminophenylalanine, 4-allylethylaminophenylalanine, 4-ethylpropylaminophenylalanine, 4-ethylisopropylaminophenylalanine, 4-ethylmethylcyclopropylaminophenylalanine, 4-(1-pyrrolidinyl)phenylalanine, 4-ethylthiomethylphenylalanine, 4-O-(2-chloroethyl)tyrosine, 3-dimethylaminophenylalanine and 3-ethylaminophenylalanine

29. Pharmaceutical composition, characterized in that it contains at least one compound

according to claim 1 or 2 which may or may not be associat d with ~~a~~ group A streptogramin.

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